Amendments to the Claims

Please cancel claims 4-5, 12-13, 23, 27-30 and 38, without prejudice.

Please amend the claims as follows:

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1. (amended) A method of imaging of an animate human or non-human animal body, which method comprises:

a) administering parenterally to said body a particulate material comprising a matrix or membrane material and at least one magnetic resonance contrast generating species wherein said magnetic resonance contrast generating species is not a gas or a gaseous precursor, ~~which~~and wherein said matrix or membrane material is responsive to a pre-selected physiological parameter and the response is an increased matrix or membrane permeability or chemical or physical breakdown of the matrix or membrane material, whereby to alter the contrast efficacy of said species in response to a change in the value of said parameter;

b) generating MR image data of at least part of said body in which said species is present; and

c) generating therefrom a signal indicative of the value or variation of said parameter in said part of said body.

D1 with

2. (amended) A method as claimed in claim 1 wherein the physiological parameter is pH, temperature, pressure, carbon dioxide tension, oxygen tension, enzyme activity, tissue electrical activity, tissue water diffusion or ion concentration.

3. (Original) A method as claimed in claim 2 wherein the physiological parameter is pH, temperature or pressure.

4. (Cancelled).

5. (Cancelled).

D2

6. (amended) A method ~~of MRI~~ as claimed in ~~5~~1, wherein the magnetic resonance contrast generating species is selected from the group consisting of ~~a~~ paramagnetic ~~compound~~compounds, ~~a~~ superparamagnetic ~~compound~~compounds, ferrimagnetic compounds, ferromagnetic compounds and compounds containing other non-zero spin nuclei than hydrogen~~an iron oxide, a gadolinium compound and a dysprosium compound~~.

7. (Cancelled).

8. (Cancelled).

9. (Original) A method as claimed in claim 1 wherein said particulate material is in combination with a targeting ligand for a cell or receptor of interest.

D3

10. (amended) A method as claimed in claim 1 wherein the matrix or membrane material forms a vesicle or a liposome.

11. (once amended) A method as claimed in claim 1 wherein the matrix or membrane material is selected from [a phospholipid]lipids, phospholipids, surfactants, proteins, oligomers or polymers~~and a physiologically acceptable polymer~~.

12. (Cancelled).

13. (Cancelled).

14. (Cancelled).

15. (Cancelled).

16. (Cancelled).

17. (Cancelled).

18. (Cancelled).

19. (Cancelled).

20. (Cancelled).

21. (Cancelled).

22. (Cancelled).

23. (Cancelled).

24. (amended) A method as claimed in claim ~~10~~48, wherein ~~the matrix or membrane material is responsive to temperature and~~ the change in the value of temperature in said animate human or non-human animal body results from external heating.

25. (Original) A method as claimed in claim 24 wherein said external heating is carried out using focused ultrasound.

D4

26. (amended) A method as claimed in claim ~~24~~47, wherein ~~the matrix or membrane material comprises a~~the lipid or lipid mixture or the phospholipid or the phospholipid mixture has a Tc value between 35°C and 80°C.

27. (Cancelled).

28. (Cancelled).

29. (Cancelled).

30. (Cancelled).

D5

31. (amended) A method as claimed in claim ~~1~~48, wherein the ~~physiological parameter is temperature and the~~ change in the value of ~~said parameter~~temperature is related to cancer, cardiovascular disease or inflammation ~~or results from external heating~~ in the animate human or non-human animal body.

D5 cont'd

32. (amended) A method as claimed in claim ~~28~~49, wherein the ~~physiological parameter is pH and wherein~~ change in the value of ~~said parameter~~pH is caused by cancer, cardiovascular disease, osteoporosis, inflammations or autoimmune diseases in the animate human or non-human animal body.

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33. (Original) A method as claimed in claim 32 wherein in addition to the generation of a signal indicative of the value or variation of a pre-determined physiological parameter in a part of the animate human or non-human animal body in which the contrast generating species is present, an anatomical image of the same part of the animate human or non-human animal body is generated.

34. (Original) A method as claimed in claim 33 wherein no contrast agent is used to generate the anatomical image.

35. (Original) A method as claimed in claim 33 wherein a contrast agent is used in the generation of the anatomical image.

36. (Original) A method as claimed in claim 30 wherein the same contrast agent is used to generate a signal relating to the pre-selected physiological parameter and the anatomical image.

37. (once amended) A contrast medium for imaging of a physiological parameter, said medium comprising a particulate material the particles whereof comprise a matrix or membrane material and at least one magnetic resonance contrast generating species with the proviso that the magnetic resonance contrast generating species is not a gas or a gaseous precursor, said matrix or membrane material being responsive to a pre-selected physiological parameter and the response is an increased matrix or membrane permeability or chemical or physical breakdown of the matrix or membrane material, to cause the contrast efficacy of said contrast generating species to vary in response to said parameter.

38. (Cancelled).

39. (new) A method as claimed in claim 6 wherein the magnetic resonance contrast generating species is a paramagnetic compound.

40. (new) A method as claimed in claim 39 wherein the magnetic resonance contrast generating species is a paramagnetic compound selected from the group consisting of stable free radicals, transition metal compounds and lanthanide metal compounds.

41. (new) A method as claimed in claim 40 wherein the magnetic resonance contrast generating species is a paramagnetic compound selected from the group consisting of manganese compounds, gadolinium chelates, ytterbium chelates, dysprosium chelates and europium compounds.

42. (new) A method as claimed in claim 6 wherein the magnetic resonance contrast generating species is a superparamagnetic metal oxide.

43. (new) A method as claimed in claim 6 wherein the magnetic resonance contrast generating species is a compound containing other non-zero spin nuclei than hydrogen selected from the group consisting of ^{19}F, ^{13}C, ^{15}N, ^{29}Si and ^{31}P.

44. (new) A method as claimed in claim 43 wherein the magnetic resonance contrast generating species is a compound containing ^{19}F.

45. (new) A method as claimed in claim 43 wherein the magnetic resonance contrast generating species is a compound containing ^{13}C or ^{15}N.

46. (new) A method as claimed in claim 43 wherein the non-zero spin nuclei are hyperpolarized nuclei.

47. (new) A method as claimed in claim 10 wherein the matrix or membrane material comprises a lipid or a lipid mixture or a phospholipid or a phospholipid mixture.

48. (new) A method as claimed in claim 47 wherein the matrix or membrane material is responsive to temperature.

49. (new) A method as claimed in claim 15 wherein the matrix or membrane material is responsive to pH.

50. (new) A contrast medium as claimed in claim 37 wherein the matrix or membrane material is responsive to pH, temperature, pressure, carbon dioxide tension, oxygen tension, enzyme activity, tissue electrical activity, tissue water diffusion or ion concentration.

51. (new) A contrast medium as claimed in claim 37 wherein the matrix or membrane material is responsive to pH, temperature or pressure.

52. (new) A contrast medium as claimed in claim 37 wherein the magnetic resonance contrast generating species is selected from the group consisting of paramagnetic compounds, superparamagnetic compounds, ferrimagnetic compounds, ferromagnetic compounds and compounds containing other non-zero spin nuclei than hydrogen.

53. (new) A contrast medium as claimed in claim 52 wherein the magnetic resonance contrast generating species is a paramagnetic compound.

54. (new) A contrast medium as claimed in claim 53 wherein the magnetic resonance contrast generating species is a paramagnetic compound selected from the group consisting of stable free radicals, transition metal compounds and lanthanide metal compounds.

55. (new) A contrast medium as claimed in claim 53 wherein the magnetic resonance contrast generating species is a paramagnetic compound selected from the group consisting of manganese compounds, gadolinium chelates, ytterbium chelates, dysprosium chelates and europium compounds.

D 7 Cont

56. (new) A contrast medium as claimed in claim 52 wherein the magnetic resonance contrast generating species is a superparamagnetic metal oxide.

57. (new) A contrast medium as claimed in claim 52 wherein the magnetic resonance contrast generating species is a compound containing other non-zero spin nuclei than hydrogen selected from the group consisting of ^{19}F, ^{13}C, ^{15}N, ^{29}Si and ^{31}P.

58. (new) A contrast medium as claimed in claim 57 wherein the magnetic resonance contrast generating species is a compound containing ^{19}F.

59. (new) A contrast medium as claimed in claim 57 wherein the magnetic resonance contrast generating species is a compound containing ^{13}C or ^{15}N.

60. (new) A contrast medium as claimed in claim 57 wherein the non-zero spin nuclei are hyperpolarized nuclei.

61. (new) A contrast medium as claimed in claim 37 wherein the matrix or membrane material is selected from lipids, phospholipids, surfactants, proteins, oligomers or polymers.

62. (new) A contrast medium as claimed in claim 57 wherein the matrix or membrane material forms a vesicle or a liposome.

63. (new) A contrast medium as claimed in claim 61 wherein the matrix or membrane material comprises a lipid or a lipid mixture or a phospholipid or a phospholipid mixture.

64. (new) A contrast medium as claimed in claim 63 wherein the matrix or membrane material is responsive to temperature.

65. (new) A contrast medium as claimed in claim 63 wherein the matrix or membrane material is responsive to pH.

66. (new) A contrast medium as claimed in claim 63 wherein the lipid or the lipid mixture or the phospholipid or the phospholipid mixture has a Tc value between 35°C and 80°C.

67. (new) A contrast medium as claimed in claim 37 wherein said particulate material is in combination with a targeting ligand for a cell or receptor of interest.

68. (new) A contrast medium as claimed in claim 37 wherein the matrix or membrane material is responsive to temperature and comprises hydrogenated phosphatidyl choline (HPC), hydrogenated phosphatidylserine-sodium (HPS), dipalmitoylphosphatidyl-choline (DPPC), distearylphosphatidylcholine (DSPC), dipalmitoylphosphatidyl glycerol (DPPG), dipalmitoyl-phosphatidylethanolamine (DPPE), dibehenoylphosphatidyl-choline, dimyristoyl-phosphatidyl glycerol (DMPG), cholesterol, cardiolipin and starch and the magnetic resonance contrast generating species is selected from the group consisting of superparamagnetic iron oxide, GdDTPA-BMA, GdBOPTA, GdDTPA, GdDOTA, GdHPDO3A, DyDTPA-BMA and PrDO3A.